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EVALUATING THE RELATIONSHIP BETWEEN DIABETES AND MENSTRUAL CYCLE IRREGULARITIES

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EVALUATING THE RELATIONSHIP BETWEEN DIABETES AND MENSTRUAL CYCLE IRREGULARITIES

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ABSTRACT

Purpose. To evaluate the relationship between menstrual cycle irregularity and several key variables, and to determine whether the odds of diabetic women self-reporting menstrual cycle irregularities is greater than non-diabetic women self-reporting menstrual cycle irregularities.
Methods. A cross-sectional study was conducted using data from the Kentucky Women's Health Registry from 2006 to 2014. The data was restricted based on age (used as a proxy for menopause status) and self-reported pregnancy and breastfeeding status, as well as eligibility to menstruate, yielding a final population of 4,256 participants for analysis. Basic statistical frequency analyses were conducted, stratified by menstrual cycle status. Bivariate analyses were conducted on the data to estimate odds ratios for menstrual irregularities based on diabetes status and adjusting for confounders. A logistic regression analysis was performed to estimate the adjusted odds women with diabetes reporting menstrual cycle irregularities.
Results. The unadjusted odds of self-reported menstrual cycle irregularities were significantly greater in diabetic than non-diabetic women (OR = 2.09, p-value <0.05). This result was no longer significant after adjusting for confounders (OR = 1.17, p-value = 0.39). When subtypes of diabetes were considered for unadjusted analyses, type II diabetics taking insulin only (OR = 2.74, p-value < 0.05), type II diabetics controlling by diet alone (OR = 2.52, p-value < 0.05), and type II diabetics taking oral pills only (OR = 2.16, p-value < 0.05) yielded the largest odds of self-reporting menstrual cycle irregularities versus non-diabetic women. In the fully-adjusted model utilizing the diabetes subtypes variable, type II diabetes controlled by diet only was significant (OR = 3.36, p-value = 0.02). The reduced adjusted model showed a strong, statistically significant increase for the dichotomous diabetes variable compared to the result from the fully-adjusted model (OR = 1.53, p-value = 0.006).
Conclusion. Results indicate a consistent relationship in self-reported menstrual cycle irregularities among diabetic women when compared with non-diabetic women. In the expanded diabetes variable model, type II diabetes controlled by diet only was significantly associated with menstrual cycle irregularities, though small numbers necessitate cautious interpretation. Multicollinearity, skewing, and bias could be impacting the results. Further analysis is needed to determine the relationship of diabetes and menstrual cycle irregularities in adult women.

Keywords: menstruation, diabetes, menstrual irregularities, menstrual disturbances, menses

INTRODUCTION

Menstrual cycle irregularities, such as oligomenorrhea or amenorrhea, are an often-overlooked aspect of women's health that carries a high patient burden. Menstrual cycles are used as a general overall indicator of women's health, and irregularities in the menstrual cycle could be indicative of several adverse conditions, such as fertility disorders.[1-3] An irregular menstrual cycle is considered to be menstrual bleeding occurring more frequently than a 21 day cycle, less frequently than 35-day cycles, or an irregular bleeding pattern (such as bleeding between periods or abnormally heavy cycles).[4] Currently, the most commonly prescribed treatments for the correction of menstrual cycle dysfunctions are various forms of hormone-based contraceptives. Considering the pharmacoeconomical aspect of the patient burden associated with adhering to a birth control regimen. For example, a 2012 study found that women living in states mandating contraceptive coverage by private insurance companies had a greater odds of adhering to a consistent schedule.[5] For these therapies to be effective, they must be taken consistently. However, costs associated with these therapeutics could play a significant role in adherence. Another 2012 study examined a population of women between ages 13 and 50 who had purchased at least one oral contraceptive pill between 1996 and 2008.[5] The data was compiled from the Medical Expenditures Panel Survey.[6] Users of combined-hormone oral contraceptive pills spent an average of $16 per pack while users of progestin-only pills spent an average of $13 per pack, yielding an average yearly expenditure of $192 and $156 respectively.[6] While the study did not explicitly state an average out-of-pocket expenditure based on insurance status, the authors noted that women with private insurance were less likely than uninsured women to pay $15 or more per pack; Medicaid enrollees saw this likelihood decrease even further.[5] A 2015 study found that this burden was significantly eased by the Affordable Care Act, increasing substantially the proportion of women with no co-pay for contraceptives[7], as well as increasing the proportion of women with insurance.

Comorbid health conditions, such as diabetes, may explain menstrual dysregulation in some women. Diabetes is one of the most common chronic diseases in the United States, and, indeed, within Kentucky. The CDC reports that 9.3% of the American population has diabetes[8], and an age-adjusted estimate of 11.3% of women in Kentucky had diabetes as of 2014.[9] This number is only expected to rise alongside the increasing obesity rate.

The relationship between diabetes and menstrual dysregulation in adult women is not well understood, given the inconsistent results from prior analyses and limited literature available on the subject. Using data from the Kentucky Women's Health Registry (KWHR), this study will characterize menstrual cycle dysregulation among adult women in Kentucky and evaluate its risk factors, emphasizing its relationship to diabetes.

Literature Review

Data on menstrual cycles are generally self-reported. Regarding the validity of the self-reported data, a 2008 study found that "on average, women overestimated their cycle length by 0.7 days".[2] Moreover, data from sexually active populations within the study were more accurate than data from unmarried women who are not sexually active.[2] The authors note this difference could be due to the need for "family planning" methods among sexually active populations.[2] Menstrual cycle irregularities have been shown to be linked to many diseases, such as metabolic disorders.[1] A 2016 Iranian study found significant risk for type 2 diabetes and pre-diabetes among women with irregular menstrual cycles when compared to women with regular menstrual cycles: the adjusted hazard ratios were 1.73 and 1.33, respectively.[1] This finding may suggest that diabetes and menstrual dysregulation share a common set of risk factors, or that disruptions in reproductive hormones may affect the endocrine system, or perhaps both.

Literature on the relationship between menstrual cycles and diabetes is limited, with most available studies focusing primarily on adolescent health and type 1 diabetes. The exact physiological relationship between the two is also not well-defined, though it seems that it hinges on gonadotropin-releasing hormone (GnRH) release.[10] A 1994 review details several possible pathophysiological relationships between menstruation and insulin-dependent diabetes, citing the impact of insulin and insulin-like growth factor-1 (IGF-1) in hormone synthesis and overall gonadal physiology.[10] Ovarian function has also been shown to not be significantly affected by diabetes in human.[10] Possible disturbances in ovarian function (such as ovarian atrophy) have been observed in diabetic animals, and progesterone production has been restored through controlled dosing with insulin.[10] The authors note, however, that "while hyperandrogenaemia may occur in women with [insulin-dependent diabetes mellitus], it is not typically a significant factor responsible for anovulation."[10] The authors also found conflicting evidence of GnRH-stimulated luteinizing hormone release due to "different methods of patient selection in various cited studies."[10] The primary physiological relationship of interest posited by the authors deals with hypothalamic function, noting a possible interruption in hypothalamic function and GnRH-release "in women with poorly controlled diabetes mellitus" while acknowledging that the exact reason for this is unclear.[10]

A 1984 study sought to determine the effect of diabetes on age at menarche among a group of 211 adolescents between 9 and 25 years of age.[11] The study found that no significant differences in menstrual cycle regularity exist between populations of non-diabetic and diabetic adolescents, but that age at menarche did seem delayed among adolescents with a diabetic onset occurring during puberty rather than before.[11] Like the 1994 study[10], this study noted the likely disruption to be due to the influence the condition has on the hypothalamic-pituitary-gonadal axis maturation in females with a diabetic onset occurring during puberty, which results in a disruption in sexual maturation.[11] It is worth noting, however, that this study suffers from significant selection bias, as the population only included white females within 20% of the ideal body weight, and is thus not generalizable to the general population. The inclusion of children who have not reached menarche may also create bias in this study.

By contrast, a 2008 Italian study of similar design, also conducted solely on white females, found age at menarche to be delayed among patients with type 1 diabetes, and found no significant association with increased HbA1c levels or BMI.[12] This study could also be influenced by significant selection bias and a lack of generalizability to the larger population. Similarly, a cross-sectional study in 2011 using NHANES data for a population of women between the ages of 12 and 24 found that "the age of menarche in adolescent females with premenarchal presentation of [type 1 diabetes mellitus] continues to be delayed."[13] This study also found that poor metabolic control (as shown by the significant negative correlation found among women with a higher BMI than women with a lower BMI regarding age at menarche) could play an important role in age at menarche.[13]

A 2015 study, however, using self-reported answers to a questionnaire for a group of women over age 18, found no significant difference in age at menarche between women with type 1 diabetes and the control group, while also failing to find any significant differences in menstrual cycle irregularities between the groups (approximately 33.2% overall for type 1 diabetics of all ages compared to approximately 30.2% in the control group, with a p-value of 0.2).[14]

A 1992 Danish study sought to characterize 570 women between ages 18 and 49 in a particular county based on menstrual cycle status, with diabetic cases ascertained using prescription records.[15] The control group was recruited through a random selection process using the registration of persons living in the county at the Odense University Hospital.[15] The researchers found a significant difference in all menstrual cycle irregularity categories analyzed (primary amenorrhea, secondary amenorrhea, and oligomenorrhea/polymenorrhea).[15] Similarly, a 1995 study by Yeshaya and colleagues of 100 diabetic patients with a mean age of 22 years, found 32% of this population reporting menstrual disturbances during the observation period, though the observation period is never clearly defined within the context of the study.[16] The primary conclusion by these authors is that menstrual disturbances are more frequent in patients with poorly controlled diabetes.[16] These authors also cite possible hypothalamic-pituitary-ovarian axis function being influenced by insulin, additionally noting that the impact of weight and body fat should not be overlooked.[16]

A 2003 study limited to women with type 1 diabetes and comparing them to their non-diabetic sisters and unrelated control subjects also found a significant increase in menstrual cycle irregularities among women with type 1 diabetes than the control groups.[17] When analyzed by age category in the univariate model, however, the results shift to statistically different menstrual irregularities being found only among type 1 diabetic women under age 20 and between ages 20 and 29, with no statistically different results found in the two other age categories (30-39 years and 40-49 years).[17] These results were echoed in their final logistic regression models, though the only results provided by the authors are odds ratios for women with type 1 diabetes, making further interpretation of the authors' results difficult.[17] The study also collapses younger women into one category, women less than 20 years of age.[17]

Utilizing HbA1c levels to determine adolescents' (age 12 to 18) diabetic control, a 2010 age-matched case-control study conducted in Greece found that both the incidence and odds of oligomenorrhea were significantly increased among women with type 1 diabetes than the controls (28.4% among the women with type 1 diabetes, compared to the 5.5% among the controls).[18] This study showed an increased prevalence of menstrual irregularities among adolescents with type 1 diabetes.[19] A similar 2010 study conducted in Santiago, Chile found that menstrual irregularities are common among adolescents, but "menstrual irregularities become more severe with poor metabolic control."[20] In this prospective study, the patients, all of whom had reached menarche and were under age 19, were asked to self-report days of menstrual cycles using a calendar which the patients were to highlight and, as in the Greek study[18], HbA1c levels were utilized to determine the extent of diabetic control.[20] However, bias cannot be excluded in this result, as the authors note that the control group was contacted monthly by telephone to fill out their calendars, while the group of girls with type 1 diabetes had their menstrual cycles recorded monthly at the hospital.[20]

Many studies also highlighted physical symptoms occurring alongside diabetes and irregular menstruation, particularly in regards to hyperandrogenism. The aforementioned 2015 study found no significant differences in self-reporting of hirsutism between the women with type 1 diabetes and the control group, with 38% of women with type 1 diabetes compared to 43% of controls.[14] In 2012, a cross-sectional study in France examined the relationship between hirsutism and menstrual irregularities in girls with either obesity or type 1 diabetes.[21] This study found significantly higher results of menstrual irregularities and symptoms of hyperandrogenism among women with elevated body mass indexes (BMIs) than among women with type 1 diabetes.[21] Another 2012 study giving an overview of the reproductive characteristics of women with type 1 diabetes in Chile found that between “20-30% of the young adult women with [type 1 diabetes]” displayed symptoms of excess androgen, which was higher than the Chilean general population (3%) and the Spanish general population (7.1%).[22] The authors also found an increased prevalence of polycystic ovarian syndrome (PCOS) in women in Chile and Spain with type 1 diabetes: among the Chilean women with type 1 diabetes, the observed prevalence was 12%, while the Spanish women with type 1 diabetes had an observed prevalence of 18.8%), compared to the prevalence in the general Spanish population, which lingers at approximately 6.5%.[22] Several of these studies note the relationship between irregular menstruation, insulin resistance, and excess androgens converging in another common endocrine disorder: PCOS.[22-23] PCOS is a disease impacting a large population of women, the exact extent of which is hard to determine due to lack of surveillance on the disease. Various estimates placed the number of women impacted by the disease anywhere between 4% and 12%.[24-26] PCOS is a disease hallmarked, in part, by the presence of insulin resistance and the oligomenorrhea or amenorrhea, though these characteristics are not necessary for the diagnosis of the disease.[26,27] This condition could also give significant insight into the exact mechanistic relationship between diabetes and menstrual cycle dysfunction, though further research is needed to determine the exact extent to which the conditions are related.

Finally, there is some indication that menstruation also affects diabetes. In a 1977 study, using interviews by physicians on patients admitted to care for ketoacidosis from January 1974 to June 1976, the researchers sought to uncover changes in insulin dosing and dietary habits in or around the patients’ menstrual cycles.[28] The authors found a significant difference in diabetic control, particularly in regards to hyperglycemia near or during the time of menstruation among the women questioned by the doctors, though a significant volume of unacknowledged recall bias may be affecting the overall results of the study.[28] A 1998 study of Pima Indian women also found that the prevalence of type 2 diabetes was higher among women who had reported menstrual cycle irregularities (at 33% compared to 24% in the controls).[23]

METHODS

A cross-sectional study design was created using data from the Kentucky Women's Health Registry (KWHR), obtained from years 2006 to 2014, contributing an initial population of 52,020 de-identified observations with 16,645 unique participants. The data was limited to years in which both pregnancy and breastfeeding data was available (2009 to 2014) and limited to the first observation from each individual in the study based on the unique ID variable assigned to them by KWHR. This created a population of 38,570 subjects, consisting of 13,632 unique participants. Women who were unable to menstruate due to self-reported conditions were excluded from the analysis; these populations included women over age 45 (considered the average age for perimenopausal women[29]), women who reported that they had been pregnant or breastfeeding within the past year (including women who suffered from ectopic pregnancies), women who had undergone a hysterectomy, and women who had both ovaries removed. Variables were not available for other medical conditions that could result in amenorrhea. Age was used as a proxy for menopause status, despite the availability of menopause data in KWHR, because of the limitations of the menopause outcomes data within the survey (C. Brancato, email correspondence, December 7, 2016). After the restriction of the data to the eligible population, 4,256 participants remained in the analysis. The University of Kentucky Institutional Review Board (IRB) approved all research activities conducted in the original KWHR. No IRB approval was required for this secondary analysis of de-identified data.

Menstrual Cycles

A dichotomous variable for self-reported menstrual cycle irregularity was utilized in the analysis, designating the participants' responses to the survey question "During the past year, have you experienced any of the following?" in which irregular menstrual cycles was an option for response. The referent group for the analysis was women indicating no menstrual cycle irregularities. Observations in which data was missing for this question was excluded from the population. A variable was available regarding length of cycle, but was not utilized due to the potential for misclassification bias based on the levels of the variable, which included options for within the past 2 months, between 2 months to 1 year, between 1-3 years, between 3-5 years, more than 5 years ago, and never had a menstrual cycle.

Diabetes

The diabetes variable included several categories of diabetes subtypes. A dichotomous variable for diabetes status was created, but the subtype variable with multiple categories was also utilized in the analysis because of the uniqueness in identifying not only different types of diabetes, but also different treatments. Diabetes was measured based on self-reported data from the survey responses, and included information on whether an observation was an insulin resistant or glucose resistant diabetic or pre-diabetic, a type I diabetic, a type II diabetic controlling the condition through diet only, a type II diabetic controlled by oral pills only, a type II diabetic taking insulin, a type II diabetic using both oral pills and insulin, unknown type of diabetes, and non-diabetic. The referent group for this population was women reporting no diabetes.

Confounders

Confounders considered for this analysis were age, weight, race and ethnicity, smoking status, type of health insurance and education level (used as a proxy for socioeconomic status), activity level, general health status, current stress level, problems controlling worry, excessive anxiety and worry, gynecological conditions such as polycystic ovarian syndrome and endometriosis, hormone therapy usage, and whether a subject was currently trying to lose weight. These confounders were measured via self-reported status. With the exception of age and weight, the variables analyzed were dichotomous. Many of the analyzed confounders were also included in similar analyses, in particular the 1992 Danish study[15] and the 1998 Pima Indian study[23]. These confounders were chosen based on their relation to menstrual cycle irregularities, and were examined within the analysis for association with diabetes.

Age, weight, race and ethnicity, smoking status, and the socioeconomic status proxy, type of health insurance and education level, are basic demographic characteristics examined for relation to both diabetes and menstrual cycle irregularities. An insurance variable was created using the dichotomous variables provided in the dataset, in which the data was categorized from federal and state issued insurance levels (Medicare or Medicaid) to private insurance. A race variable was also created, utilizing the dichotomous race variables and the variable for primary race in instances where more than one race was identified by the participant. A participant was categorized in a race category if they marked only one race in the dichotomous variable level or identified a primary race in the leveled variable. The creation of this variable resulted in 4 observations lost from the study, as not all participants identified a primary race. BMI was utilized over the weight variable to account for theoretical adiposity and weight distribution.[31] Weight was assessed as a potential effect modifier.[12, 15, 30] A categorical variable for BMI was created based on WHO standards: a BMI over 25 was considered overweight, while a BMI under 18.5 was considered underweight.[30-33]

Activity level, current stress level, problems controlling worry, excessive anxiety and worry, and whether a woman was currently trying to lose weight all are known to impact menstrual cycle regularity. General health status, other gynecological conditions, and hormone usage were considered because of their relationship with menstrual cycle regularity, since, as noted earlier, menstrual cycle regularity is often used as a proxy for overall gynecological health.

Data was available for several different types of birth control currently being utilized by the women in the survey, including tubal ligation, emergency contraceptives, Implanon, Norplant implants, Depo Provera, Mirena/Paragard, birth control patches, and birth control pills. A new variable was created, indicating whether the method of birth control was likely to provoke regular menstrual cycles (birth control pills and birth control patches), unlikely to impact menstrual cycles (tubal ligation[34], emergency contraceptives[35], and Norplant implants[36]), or likely to eliminate menstrual cycles (Mirena/Paragard[37], Implanon[38], and Depo Provera[39]). Information on other birth control methods, such as Nuvaring, was not available for analysis. This multi-leveled variable was utilized for analysis over the individual dichotomous variables for each of the birth control variable due to small numbers in each of the dichotomous variables. Hormone usage was also combined into a dichotomous variable, due to small numbers in the cells for the individual dichotomous variables.

Statistical Analyses

Basic statistical descriptors of the data were obtained using frequency analyses to analyze the data based on menstrual cycle status. Analyses using the dichotomous variable for menstrual cycle irregularities and the dichotomous variable for diabetes were conducted to create frequency tables to characterize the data and distinguish differences between the two variables. Confounders were assessed using chi-square analyses for categorical variables and a Student's t-test for continuous variables to examine the strength of the factor in relation to both diabetes and menstrual cycle irregularities. Bivariate analyses were conducted on the data to determine the odds of menstrual cycle irregularities based on diabetes status and the confounders. The Breslow-Day test was utilized to examine potential effect modifiers. Logistic regression analyses were then conducted to test the hypothesis that diabetes is associated with menstrual cycle irregularities. Sensitivity analyses were conducted using stratified logistic regression analyses to examine associations of interest. Statistical analyses for this study were conducted using SAS v9.4. A significance level of 0.05 was used.

RESULTS

After exclusions, 4,256 unique participants remained in the dataset for analysis. This overall sample had a mean age of 33.63 (SD 6.74), with 27.68% (n=1,178) reporting menstrual cycle irregularities. Of the total sample, 5.92% (n=252) reported having been diagnosed with diabetes. Table 1 displays demographic information. No differences were observed between with and without menstrual cycle irregularities by age, race, or ethnicity, and the distribution of education was similar between groups. The women in the study population were overwhelmingly white and non-Hispanic.

Insurance status and education level were, together, utilized as a proxy for socioeconomic status, and both were showing to be highly significantly associated with menstrual cycle irregularities. Women reporting menstrual cycle irregularities had a larger prevalence of no insurance than women reporting no menstrual cycle irregularities (OR=1.56). Women reporting menstrual cycle irregularities also had lower education in the overall sample than women reporting no menstrual cycle irregularities. There was also a larger number of women reporting smoking more than 100 cigarettes in their lifetime (ever smoking) among the women reporting the presence of menstrual cycle irregularities than among women reporting no menstrual cycle irregularities.

Table 1. Demographic characteristics of Kentucky Women's Health Registry participants, 2009-2014, stratified by menstrual cycle regularity status (N = 4,256)

Characteristic	**Menstrual Cycle Irregularities Present n = 1,178**	**Menstrual Cycle Irregularities Absent n = 3,078**	**Odds Ratio**	**95% Confidence Interval**
Age, mean(SD)	33.22 (6.79)	33.79 (6.72)	**0.99**	**(0.98, 0.999)**
Education Level, n (%)				
High school diploma or less	51 (4.34)	132 (4.29)	1.15	(0.82, 1.60)
GED	16 (1.36)	33 (1.07)	1.44	(0.79, 2.63)
Vocational or training certificate	45 (3.83)	100 (3.25)	1.34	(0.93, 1.92)
Some college or associate's degree	**345 (29.34)**	**678 (22.05)**	**1.51**	**(1.29, 1.77)**
Bachelor's degree or higher	690 (58.67)	2,048 (66.60)	*Ref*	--
Other	29 (2.47)	84 (2.73)	1.03	(0.67, 1.58)
Missing	2	3		
Race, n (%)				
White	1,118 (95.31)	2,879 (94.39)	*Ref*	--
Black/African-American	34 (2.90)	122 (4.00)	0.72	(0.49, 1.06)
Asian	8 (0.68)	26 (0.85)	0.79	(0.36, 1.76)
American Indian or Alaska Native	5 (0.43)	8 (0.26)	1.61	(0.53, 4.93)
Native Hawaiian or Pacific Islander	2 (0.17)	4 (0.13)	1.288	(0.24, 7.04)
Other race	6 (0.51)	11 (0.36)	1.41	(0.52, 3.81)
Missing	5	28		
Ethnicity, n (%)				
Hispanic	10 (0.87)	25 (0.83)	1.04	(0.50, 2.17)
Not Hispanic	1,145 (99.13)	2,972 (99.17)	*Ref*	--
Missing	23	81		
BMI, mean (SD)	29.09 (8.62)	27.50 (7.14)	**1.03**	**(1.02, 1.04)**
Missing	37	101		
BMI Category, n (%)				
Underweight	24 (2.10)	49 (1.65)	1.44	(0.88, 2.38)
Normal weight	446 (39.09)	1,315 (44.17)	*Ref*	--
Overweight	671 (58.81)	1,613 (54.18)	**1.23**	**(1.07, 1.41)**
Missing	37	101		

Table 1. Continued.

Insurance, n (%)				
Medicare/Medicaid	41 (3.51)	72 (2.35)	**1.61**	**(1.09, 2.38)**
VA/Tricare	22 (1.88)	36 (1.18)	**1.73**	**(1.01, 2.96)**
Private insurance	945 (80.91)	2,676 (87.45)	*Ref*	--
Uninsured	147 (12.59)	247 (8.07)	**1.69**	**(1.36, 2.10)**
Unknown	13 (1.11)	29 (0.95)	1.27	(0.66, 2.45)
Missing	10	18		
Smoking status, n (%)				
Never smoker	758 (64.68)	2,115 (69.30)	*Ref*	--
Every day smoker	144 (12.29)	266 (8.72)	**1.51**	**(1.21, 1.88)**
Some days smoker	54 (4.61)	128 (4.19)	1.17	(0.85, 1.64)
Used to smoke, but quit	216 (18.43)	543 (17.79)	1.11	(0.93, 1.33)
Missing	6	26		

Key demographic figures for the Kentucky Women's Health Registry population, stratified by menstrual cycle regularity status, represent crude associations for age, BMI both as a continuous variable and a categorical variable, education, insurance status, race and ethnicity, and smoking status. Of these variables, age, BMI (both continuous and categorical), and insurance status were significant.

Of the women reporting presence of menstrual cycle irregularities, 9.25% (n=109) of women reported diabetes, compared to 4.65% (n=143) of women reporting no menstrual cycle irregularities (p-value <.0001, OR=2.09) (Table 2). Among the women reporting diabetes for both groups, insulin resistant, glucose intolerant, or pre-diabetic women held the largest percentage of observations (4.07% among women reporting menstrual cycle irregularities and 2.08% among women reporting no menstrual cycle irregularities). Type II diabetic women taking insulin alone had the highest odds of self-reporting menstrual cycle irregularities, with these women having odds 2.74 times higher than non-diabetic women.

Table 2. Crude association between menstrual cycle irregularities and diabetes, Kentucky Women's Health Registry, 2009-2014.

Variable	Menstrual Cycle Irregularities Present n = 1,178	Menstrual Cycle Irregularities Absent n = 3,078	Odds Ratio	95% Confidence Interval
Diabetes, n(%)	109 (9.25)	143 (4.65)	**2.09**	**(1.62, 2.72)**
Diabetes Subtypes, n (%)				
Insulin resistant, glucose intolerant, or pre-diabetic	48 (4.07)	64 (2.08)	**2.06**	**(1.41, 3.02)**
Type I diabetic	9 (0.76)	16 (0.52)	1.55	(0.68, 3.51)
Type II diabetic, diet only	11 (0.93)	12 (0.39)	**2.52**	**(1.11, 5.72)**
Type II diabetic, oral pills only	26 (2.21)	33 (1.07)	**2.16**	**(1.29, 3.64)**
Type II diabetic, insulin only	8 (0.68)	8 (0.26)	**2.74**	**(1.03, 7.33)**
Type II diabetic, oral pills and insulin	3 (0.24)	5 (0.16)	1.65	(0.39, 6.91)
Unknown diabetic	4 (0.34)	5 (0.16)	2.20	(0.59, 8.20)
Non-diabetic	1069 (90.75)	2935 (95.35)	*Ref*	--

Diabetes is shown to be significantly associated with menstrual cycle irregularity status in these frequency analyses with bivariate odds ratios.

As noted earlier, menstrual cycle irregularities are often indicative of other gynecological issues, and, as such, may be important potential confounders.[1-3] Table 3 presents self-reported diagnoses of these conditions stratified by menstrual cycle regularity status. Many of these variables, unsurprisingly, showed significant differences among the groups. In each case, the conditions are reported by women with menstrual cycle irregularities by a ratio of as much as two to three times higher than women reporting no menstrual cycle irregularities. The constructed birth control variable showed significant differences, with the largest differences being shown in birth control likely to provoke menstrual cycles. Curiously, hormone usage was shown to have no significant differences among the strata, most likely due to a large percentage of the data being missing (approximately 46% of the observations) and small numbers in each of the cells.

Table 3. Diagnosed gynecological conditions of Kentucky Women's Health Registry participants, 2009-2014, stratified by menstrual cycle regularity status (N = 4,256).

Variable	Menstrual Cycle Irregularities Present n = 1,178	Menstrual Cycle Irregularities Absent n = 3,078	Odds Ratio	95% Confidence Interval
Abnormal Pap Smear, n (%)	370 (31.54)	855 (27.83)	**1.20**	**(1.03, 1.38)**
Missing	5	6		
Endometriosis, n (%)	110 (9.38)	235 (7.65)	1.25	(0.99, 1.58)
Missing	5	6		
Endometriosis Removed, n (%)	34 (5.02)	82 (4.90)	1.03	(0.68, 1.55)
Missing	501	1,403		
Fibroid Diagnosis, n (%)	81 (6.91)	164 (5.34)	1.32	(0.999, 1.73)
Missing	5	6		
Frequent Vaginal Infections, n(%)	49 (4.16)	84 (2.73)	**1.55**	**(1.08, 2.22)**
Missing	5	6		
Frequent Yeast Infections, n (%)	113 (9.63)	229 (7.45)	**1.32**	**(1.04, 1.68)**
Missing	5	6		
General pelvic pain, n (%)	166 (14.09)	223 (7.24)	**2.10**	**(1.70, 2.60)**
Infertility, n (%)	105 (8.95)	141 (4.59)	**2.05**	**(1.57, 2.66)**
Missing	*S*5	6		
Low sex drive, n (%)	529 (44.91)	1,133 (36.81)	**1.40**	**(1.22, 1.60)**
Painful or prolonged menstrual cycles, n (%)	709 (60.19)	1,455 (47.27)	**1.69**	**(1.47, 1.93)**
Pain with intercourse, n (%)	365 (22.50)	425 (13.81)	**1.81**	**(1.53, 2.15)**
Pelvic adhesions, n (%)	17 (1.45)	20 (0.65)	**2.25**	**(1.17, 4.30)**
Missing	5	6		
PMS/PMDD, n (%)	145 (12.36)	292 (9.51)	**1.34**	**(1.09, 1.66)**
Missing	5	6		
Polycystic ovarian syndrome, n (%)	144 (12.28)	160 (5.21)	**2.55**	**(2.01, 3.23)**
Missing	5	6		
Prolonged/heavy menses, n (%)	388 (32.94)	601 (19.53)	**2.03**	**(1.74, 2.35)**
One ovary removed, n (%)	17 (1.45)	49 (1.60)	0.91	(0.52, 1.58)
Missing	4	8		
Severe hot flashes, n (%)	118 (10.02)	136 (4.42)	**2.41**	**(1.86, 3.11)**
Uterine prolapse, n (%)	3 (0.25)	11 (0.36)	0.71	(0.20, 2.56)
Missing	5	6		
Uterine polyps, n (%)	20 (1.71)	30 (0.98)	1.76	(1.00, 3.11)
Missing	5	6		
Vaginal dryness, n (%)	241 (20.46)	453 (14.72)	**1.49**	**(1.25, 1.77)**
Vulvar pain, n (%)	86 (7.30)	122 (3.96)	**1.91**	**(1.44, 2.54)**
Other diagnosed gynecological conditions, n (%)	42 (3.58)	60 (1.95)	**1.87**	**(1.25, 2.78)**
Missing	5	6		
Birth control level, n (%) †				
No birth control	587 (53.31)	1,588 (53.72)	*Ref*	--
Likely to provoke menstruation	305 (27.80)	1,011 (34.20)	**0.82**	**(0.70, 0.96)**
Likely to eliminate menstruation	157 (14.31)	227 (7.68)	**1.87**	**(1.50, 2.34)**
Not likely to impact menstruation	48 (4.38)	130 (4.40)	1.00	(0.71, 1.41)
Missing	81	122		

Table 3. Continued.

Hormone usage, n (%)*	21 (3.27)	35 (2.14)	1.54	(0.89, 2.67)
Missing	535	1,443		
How Long Between Cycles, n (%)				
Within past 2 months	997 (85.00)	2821 (92.31)	*Ref*	--
Between 2 months to 1 year	120 (10.23)	78 (2.55)	**4.35**	**(3.24, 5.84)**
Between 1-3 years	43 (3.67)	77 (2.52)	**1.58**	**(1.08, 2.31)**
Between 3-5 years ago	9 (0.77)	44 (1.44)	0.58	(0.28, 1.19)
More than 5 years ago	4 (0.34)	36 (1.18)	**0.32**	**(0.11, 0.89)**
Missing	5	22		

† Leveled birth control variable was created using dichotomous variables for different methods of birth control. Self-reported use of birth control pills or birth control patches was assigned to the "likely to provoke menstruation" category; self-reported use of Mirena or Paragard, Implanon, or Depo Provera was assigned to the "likely to eliminate menstruation" category; and self-reported tubal ligation and emergency contraceptive usage was assigned to the "not likely to impact menstruation" category. No women reported use of Norplant implants, and so the variable was not included in this leveled variable.
** Hormone usage refers to any reported use of a hormone, including hormones designed to treat infertility.*

Activity level, general health status, stress level, worry level, and anxiety levels were also stratified by menstrual cycle status (Table 4). Women reporting menstrual cycle irregularities reported lower levels of activity, worse health, and more stress than women reporting no menstrual cycle irregularities; these women also reported larger percentages of uncontrolled worry or excessive anxiety, as well as larger percentages of post-traumatic stress disorder (PTSD). Women self-reporting menstrual cycle irregularities had 3.84 times the odds of reporting poor vs. excellent overall health status compared to women reporting no menstrual cycle irregularities.

Table 4. Psychosocial health conditions of Kentucky Women's Health Registry participants, 2009-2014, stratified by menstrual cycle regularity status (N = 4,256).

Variable	**Menstrual Cycle Irregularities Present n = 1,178**	**Menstrual Cycle Irregularities Absent n = 3,078**	**Odds Ratios**	**95% Confidence Interval**
Level of physical activity, n (%)				
Sedentary	290 (24.74)	607 (19.77)	**1.58**	**(1.26, 1.97)**
Moderately active	719 (61.35)	1,929 (62.72)	**1.23**	**(1.01, 1.50)**
Very active	163 (13.91)	538 (17.52)	*Ref*	--
Missing	6	7		
General health condition, n (%)				
Excellent	149 (12.66)	551 (17.91)	*Ref*	--
Very good	453 (38.49)	1,400 (45.50)	1.20	(0.97, 1.48)

Table 4. Continued.

Good	401 (34.07)	880 (28.60)	**1.69**	**(1.36, 2.09)**
Fair	147 (12.49)	220 (7.15)	**2.47**	**(1.87, 3.26)**
Poor	27 (2.29)	26 (0.84)	**3.84**	**(2.18, 6.78)**
Missing	1	1		
Current stress level, n (%)				
Small	148 (12.57)	550 (17.91)	*Ref*	--
Moderate	545 (46.30)	1,584 (51.58)	**1.28**	**(1.04, 1.57)**
Large	361 (30.67)	749 (24.39)	**1.79**	**(1.44, 2.23)**
Overwhelming	123 (10.45)	188 (6.12)	**2.43**	**(1.82, 3.25)**
Missing	1	7		
Problems controlling worry, n (%)				
Yes, in the past 12 months	416 (45.61)	849 (39.23)	**1.32**	**(1.08, 1.62)**
Yes, in my lifetime	309 (33.88)	810 (37.43)	1.03	(0.83, 1.28)
No	187 (20.50)	505 (23.34)	*Ref*	--
Missing	266	914		
Excessive anxiety or worry, n(%)				
Yes, in the past 12 months	558 (47.65)	1,169 (38.12)	**1.65**	**(1.40, 1.96)**
Yes, in my lifetime	347 (29.63)	976 (31.82)	**1.23**	**(1.03, 1.48)**
No	266 (22.72)	922 (30.06)	*Ref*	--
Missing	7	11		
PTSD, n(%)	348 (29.82)	680 (22.27)	**1.48**	**(1.27, 1.72)**
Missing	11	25		
Trying to Lose Weight, n(%)	790 (67.69)	1,951 (63.76)	**1.19**	**(1.03, 1.37)**
Missing	11	18		

Crude associations for psychosocial health factors with menstrual cycle regularity status. Of the variables analyzed, level of physical activity, general health condition, current stress level, excessive anxiety or worry, PTSD, and trying to lose weight were shown to be significantly associated with menstrual cycle regularity status.

To further assess potential confounders, the population was then stratified based on self-reported diabetes status. Variables that showed significant associations with menstrual dysregulation were analyzed for associations with diabetes (Table 5). Diabetic women in this analysis were shown to have an average age significantly older than non-diabetic women (36.16 for diabetic women compared to 33.47 for non-diabetic women). Women with diabetes also had a larger percentage with a BMI classifying them as overweight than non-diabetic women.

Table 5. Demographic and psychosocial factors of the Kentucky Women's Health Registry participants, 2009-2014, stratified by dichotomous diabetes status (N = 4,256).

Variable	Diabetic Status (All Types) n = 252	Non-Diabetic Status n = 4013	Odds Ratio	95% Confidence Interval
Irregular menstrual cycles, n(%)	109 (43.25)	1,069 (26.70)	**2.09**	**(1.62, 2.71)**
How Long Between Cycles, n (%)				
Within past 2 months	211 (84.06)	3,607 (90.67)	*Ref*	--
Between 2 months to 1 year	22 (8.76)	176 (4.42)	**2.14**	**(1.34, 3.40)**
Between 1-3 years	11 (4.38)	109 (2.74)	1.73	(0.91, 3.26)
Between 3-5 years	5 (1.99)	48 (1.21)	1.78	(0.70, 4.5)
More than 5 years	2 (0.80)	38 (0.96)	0.90	(0.22, 3.76)
Missing	1	26		
Age, mean(SD)	36.16 (6.25)	33.47 (6.47)	**1.06**	**(1.04, 1.09)**
BMI, mean(SD)	35.75 (9.31)	27.46 (7.22)	**1.03**	**(1.02, 1.04)**
BMI Category, n (%)				
Underweight	1 (0.42)	72 (1.86)	0.96	(0.13, 7.22)
Normal weight	25 (10.46)	1,736 (44.75)	*Ref*	--
Overweight	213 (89.12)	2,071 (53.39)	**7.14**	**(4.70, 10.86)**
Missing	13	125		
Insurance, n (%)				
Medicare/Medicaid	16 (6.35)	97 (2.44)	**2.88**	**(1.67, 4.99)**
VA/Tricare	2 (0.79)	56 (1.41)	0.62	(0.15, 2.58)
Private insurance	196 (77.78)	3,425 (86.14)	*Ref*	--
Uninsured	37 (14.68)	357 (8.98)	**1.81**	**(1.25, 2.62)**
Unknown	1 (0.40)	41 (1.03)	0.43	(0.06, 3.12)
Missing	0	28		
Education Level, n (%)				
High school diploma or less	15 (5.95)	168 (4.20)	**1.87**	**(1.07, 3.26)**
GED	4 (1.59)	45 (1.13)	1.86	(0.66, 5.25)
Vocational or training certificate	16 (6.35)	129 (3.23)	**2.59**	**(1.50, 4.49)**
Some college or associate's degree	84 (33.33)	939 (23.48)	**1.87**	**(1.40, 2.49)**
Bachelor's degree or higher	125 (49.60)	2,613 (65.34)	*Ref*	--
Other	8 (3.17)	105 (2.63)	1.59	(0.76, 3.34)
Missing	0	5		
Smoking Status, n(%)				
Never smoker	164 (65.08)	2,709 (68.20)	*Ref*	--
Every day smoker	28 (11.11)	382 (9.62)	1.21	(0.80, 1.83)
Some days smoker	10 (3.97)	172 (4.33)	0.96	(0.50, 1.85)
Used to smoke, but quit	50 (19.84)	709 (17.85)	1.17	(0.84, 1.62)
Missing	0	32		

Crude associations for associations for demographic and psychosocial health factors stratified by dichotomous diabetes status. For these variables, age, BMI, and education were shown to be significantly associated with diabetes.

Table 6 stratified diagnosed gynecological conditions by diabetes status, based on the variables showing significant differences in menstrual cycle stratification from Table 3. From these analyses, abnormal pap smears, frequent vaginal infections, low sex drive, pain with intercourse, pelvic adhesions, and uterine polyps showed no significant differences between the women with and without diabetes. Many of the significant associations shown in this analysis could be due, in part, to low numbers in the diabetic strata. Fascinatingly, from Table 3, women self-reporting menstrual cycle irregularities had 2.55 times the odds of reporting a PCOS diagnosis compared to women reporting no menstrual cycle irregularities, while diabetic women had 9.18 times the odds of reporting a PCOS diagnosis compared to non-diabetic women. However, many of the associations, particularly with gynecological conditions such as polycystic ovarian syndrome, could be explained through a relationship between these conditions and adiposity.

Table 6. Diagnosed gynecological conditions of the Kentucky Women's Health Registry, stratified by diabetes status. (N = 4,256)

Variable	Diabetic Status (All Types) n = 252	Non-Diabetic Status n = 4013	Odds Ratio	95% Confidence Interval
Abnormal pap smear, n(%)	65 (25.79)	1,160 (29.05)	0.85	(0.64, 1.14)
Missing	0	11		
Frequent vaginal infections, n(%)	11 (4.37)	122 (3.06)	1.45	(0.77, 2.72)
Missing	0	11		
Frequent yeast infections, n(%)	45 (17.86)	297 (7.44)	**2.71**	**(1.92, 3.81)**
Missing	0	11		
General pelvic pain, n(%)	43 (17.06)	346 (8.64)	**2.18**	**(1.54, 3.08)**
Infertility, n(%)	34 (13.49)	212 (5.31)	**2.78**	**(1.89, 4.10)**
Missing	0	11		
Low sex drive, n(%)	104 (41.27)	1,558 (38.91)	1.10	(0.85, 1.43)
Painful or prolonged menstrual cycles, n(%)	154 (61.11)	2,010 (50.20)	**1.56**	**(1.20, 2.02)**
Pain with intercourse, n(%)	50 (19.84)	640 (15.98)	1.30	(0.94, 1.79)
Pelvic adhesions, n(%)	3 (1.19)	34 (0.85)	1.41	(0.43, 4.60)
Missing	0	11		
PMS/PMDD, n(%)	44 (17.46)	393 (9.84)	**1.94**	**(1.38, 2.73)**
Missing	0	11		
Polycystic ovarian syndrome, n(%)	87 (34.52)	217 (5.43)	**9.18**	**(6.84, 12.31)**
Missing	0	11		
Prolonged/heavy menses, n(%)	97 (38.49)	892 (22.28)	**2.18**	**(1.68, 2.84)**
Severe hot flashes, n(%)	32 (12.70)	222 (5.54)	**2.48**	**(1.67, 3.68)**

Table 6. Continued.

Uterine polyps, n(%)	4 (1.59)	46 (1.15)		
Missing	0	11		
Vaginal dryness, n(%)	55 (21.83)	639 (15.96)	**1.47**	**(1.08, 2.01)**
Vulvar pain, n(%)	19 (7.54)	189 (4.72)	**1.65**	**(1.01, 2.69)**
Other diagnosed gynecological conditions, n(%)	11 (4.37)	91 (2.28)	**1.96**	**(1.03, 3.71)**
Missing	0	11		
Birth control level, n (%)†				
No birth control	133 (58.59)	2,042 (53.37)	*Ref*	--
Likely to provoke menstruation	54 (23.79)	1,262 (32.98)	**0.66**	**(0.48, 0.91)**
Likely to eliminate menstruation	17 (7.49)	367 (9.59)	0.71	(0.42, 1.19)
Not likely to impact menstruation	23 (10.13)	155 (4.05)	**2.28**	**(1.42, 3.65)**
Missing	25	178		

† Leveled birth control variable was created using dichotomous variables for different methods of birth control. Self-reported use of birth control pills or birth control patches was assigned to the "likely to provoke menstruation" category; self-reported use of Mirena or Paragard, Implanon, or Depo Provera was assigned to the "likely to eliminate menstruation" category; and self-reported tubal ligation and emergency contraceptive usage was assigned to the "not likely to impact menstruation" category. No women reported use of Norplant implants, and so the variable was not included in this leveled variable.

Significant non-gynecological conditions from the analysis for the population stratified based on diabetes status, as shown in Table 7. Diabetic women were more likely to report themselves as being less active than non-diabetic women and in a worse general health condition, with odds of 15.13 for self-reporting fair overall health status and 35.48 for self-reporting poor overall health status. They also reported higher levels of stress, more uncontrolled worry, more excessive anxiety, and a larger percentage was trying to lose weight than among non-diabetic women. The significance of these variables could be due in part, again, to the relatively small number of diabetic women in the study population.

Table 7. Non-gynecological conditions of the Kentucky Women's Health Registry, stratified by diabetes status. (N = 4,256)

Variable	Diabetes (All Types) n = 252	No Diabetes n = 4013	Odds Ratio	95% Confidence Interval
Level of activity, n (%)				
Sedentary	94 (37.30)	803 (20.12)	**3.79**	**(2.34, 6.15)**
Moderately active	137 (54.37)	2,508 (62.84)	**1.77**	**(1.11, 2.82)**
Very active	21 (8.33)	680 (17.04)	*Ref*	--
Missing	0	13		

Table 7. Continued.

General health condition, n (%)				
Excellent	10 (3.97)	690 (17.24)	*Ref*	--
Very good	50 (19.84)	1,803 (45.05)	1.91	(0.97, 3.80)
Good	108 (42.86)	1,173 (29.31)	**6.35**	**(3.30, 12.22)**
Fair	66 (26.19)	301 (7.52)	**15.13**	**(7.67, 29.82)**
Poor	18 (7.14)	35 (0.85)	**35.48**	**(15.25, 82.55)**
Missing	0	2		
Current stress level, n (%)				
Small	24 (9.52)	674 (16.87)	*Ref*	--
Moderate	112 (44.44)	2,017 (50.48)	1.56	(0.99, 2.44)
Large	75 (29.76)	1,035 (25.90)	**2.04**	**(1.27, 3.26)**
Overwhelming	41 (16.27)	270 (6.76)	**4.27**	**(2.53, 7.20)**
Missing	0	8		
Problems controlling worry, n (%)				
Yes, in the past 12 months	106 (50.24)	1,159 (40.45)	**1.89**	**(1.26, 2.83)**
Yes, in my lifetime	73 (34.60)	1,046 (36.51)	1.44	(0.94, 2.21)
No	32 (15.17)	660 (23.04)	*Ref*	--
Missing	41	1,139		
Excessive anxiety or worry, n (%)				
Yes, in the past 12 months	134 (53.59)	1,593 (39.95)	**2.14**	**(1.51, 3.02)**
Yes, in my lifetime	72 (28.69)	1,251 (31.38)	1.46	(0.999, 2.14)
No	45 (17.93)	1,143 (28.67)	*Ref*	--
Missing	1	17		
PTSD, n(%)	72 (28.92)	956 (24.07)	1.28	(0.97, 1.70)
Missing	3	33		
Trying to Lose Weight, n (%)	202 (80.48)	2,539 (63.86)	**2.33**	**(1.70, 3.21)**
Missing	1	28		

Crude associations for non-gynecological factors stratified by diabetic status. Of the variables analyzed within this table, level of activity, general health condition, current stress level, and trying to lose weight was significantly associated with diabetes.

Based on the results from these analyses, the factors included as confounders in this analysis were age, BMI, insurance status, education level, frequent yeast infections, general pelvic pain, infertility, painful menstruation, PMS/PMDD, polycystic ovarian syndrome, prolonged/heavy menses, severe hot flashes, vaginal dryness, vulvar pain, other diagnosed gynecological conditions, birth control level, level of activity, general health condition, current stress level, problems controlling worry, excessive anxiety or worry, and trying to lose weight.

Effect Modification

The categorical BMI and birth control level variable were tested against diabetes and irregular menstrual cycles to measure effect modification. A Breslow-Day test was utilized to test for significant differences between the odds ratios. The Breslow-Day test reported a p-value for the analysis stratified by BMI of 0.29 and, for the analysis stratified by birth control level, a p-value of 0.16. Based on these tests, no evidence of significant differences between odds ratios could be justified. The variables were utilized in the logistic regression model as confounders rather than effect modifiers. Cross-products were also run using the dichotomous diabetes variable to test for interactions between the variable of interest and the variables in the model. Overwhelmingly, the results of this analysis indicated no interactions, with the exception of a couple strata of the education variable. From this, and the results of the Breslow-Day test, we conclude there is not sufficient evidence of effect modification in the context of this analysis.

Logistic Regression Analysis

Two logistic regression models were fitted to the data, first incorporating the dichotomous diabetes variable used throughout this analysis and then using the diabetes subtypes variable to gain further insight into the effect of menstrual cycle irregularity on diabetes given the confounders discovered. Table 8 shows the results of the logistic regression analysis utilizing the dichotomous diabetes variable. Significance is indicated in this table using a bold font. In this analysis, diabetes was not significantly associated with menstrual dysregulation. This could be due to the number of confounders assessed in the model, as well as multicollinearity resulting from several variables that are similar in nature. The adjusted odds ratio for diabetic women self-reporting menstrual cycle regularities was 1.17 (CI 0.82 – 1.66), indicating greater odds of diabetic women self-reporting menstrual cycle irregularities. Very few of the assessed confounders showed significance in this model.

Table 8. Logistic regression analysis and adjusted odds ratios utilizing the dichotomous diabetes variable, Kentucky Women's Health Registry, 2009-2014.

Variable	**Beta Estimate**	**Odds Ratio**	**95% CI**	**Pr > ChiSq**
Diabetes Status	0.15	1.17	(0.82, 1.66)	0.39
Age, 1-year	**-0.01**	**0.99**	**(0.97, 1.00)**	**0.04**
BMI Category				
Underweight	0.16	1.17	(0.59, 2.32)	0.65
Normal Weight	*Ref*	--	--	--
Overweight	-0.13	0.88	(0.71, 1.08)	0.21
Insurance				
Medicare/Medicaid	0.07	1.07	(0.64, 1.79)	0.80
VA/Tricare	0.50	1.65	(0.85, 3.18)	0.14
Private Insurance	*Ref*	--	--	--
Uninsured	0.24	1.28	(0.95, 1.71)	0.10
Unknown	-0.004	1.00	(0.95, 1.71)	0.99
Education Level				
High school diploma or less	0.03	1.03	(0.64, 1.66)	0.90
GED	0.01	1.01	(0.47, 2.16)	0.98
Vocational or training certificate	0.14	1.15	(0.71, 1.85)	0.58
Some college or associate's degree	**0.23**	**1.26**	**(1.02, 1.55)**	**0.03**
Bachelor's degree or higher	*Ref*	--	--	--
Other	0.05	1.05	(0.60, 1.84)	0.86
Level of Activity				
Sedentary	0.03	1.03	(0.76, 1.40)	0.85
Moderately Active	-0.03	0.97	(0.75, 1.26)	0.84
Very Active	*Ref*	--	--	--
General Health Condition				
Excellent	*Ref*	--	--	--
Very Good	0.02	1.02	(0.76, 1.35)	0.92
Good	0.20	1.22	(0.89, 1.67)	0.22
Fair	0.34	1.40	(0.94, 2.10)	0.10
Poor	0.54	1.71	(0.80, 3.68)	0.17
Current Stress Level				
Small	*Ref*	--	--	--
Moderate	0.12	1.12	(0.84, 1.51)	0.44
Large	0.26	1.30	(0.95, 1.78)	0.11
Overwhelming	0.42	1.52	(1.02, 2.26)	0.04
Problems Controlling Worry				
Yes, in the past 12 months	-0.12	0.89	(0.67, 1.17)	0.39
Yes, in my lifetime	-0.12	0.89	(0.70, 1.13)	0.33
No	*Ref*	--	--	--
Excessive Anxiety or Worry				
Yes, in the past 12 months	-0.13	0.88	(0.37, 2.08)	0.77
Yes, in my lifetime	-0.17	0.84	(0.36, 1.98)	0.70

Table 8. Continued.

No	*Ref*	--	--	--
Trying to Lose Weight	0.12	1.12	(0.92, 1.37)	0.25
Frequent Yeast Infections	-0.04	0.96	(0.71, 1.29)	0.79
General Pelvic Pain	0.22	1.25	(0.95, 1.64)	0.12
Infertility	**0.61**	**1.83**	**(1.28, 2.62)**	**0.0008**
Painful or Prolonged Menstrual Cycles	**0.27**	**1.31**	**(1.07, 1.59)**	**0.008**
PMS/PMDD	0.04	1.04	(0.80, 1.36)	0.75
Polycystic Ovarian Syndrome	**0.52**	**1.68**	**(1.21, 2.35)**	**0.002**
Prolonged/Heavy Menses	**0.36**	**1.43**	**(1.16, 1.76)**	**0.0006**
Severe Hot Flashes	**0.58**	**1.78**	**(1.28, 2.48)**	**0.0006**
Vaginal Dryness	**0.26**	**1.30**	**(1.04, 1.62)**	**0.02**
Vulvar Pain	0.31	1.36	(0.95, 1.94)	0.09
Other Gynecological Conditions	0.31	1.37	(0.81, 2.30)	0.24
Birth Control Level				
No birth control	*Ref*	--	--	--
Likely to provoke menstruation	-0.06	0.94	(0.77, 1.16)	0.56
Likely to eliminate menstruation	**0.74**	**2.10**	**(1.58, 2.79)**	**<.0001**
Not likely to impact menstruation	-0.13	0.88	(0.58, 1.34)	0.55

In this fully-adjusted logistic regression analysis model, diabetes failed to achieve statistical significance. Infertility, painful or prolonged menstrual cycles, PCOS, prolonged or heavy menses, severe hot flashes, and vaginal dryness managed to achieve statistical significance.

This analysis was then repeated utilizing the diabetes subtypes variable. The results of this analysis are shown in Table 9. Significance from this analysis are again indicated by bolded font. Type II diabetes controlled by diet alone was statistically significant in this model, with an odds ratio of 3.36 compared to non-diabetic women (p-value of 0.02). Overwhelming stress was shown to be statistically significant, increasing the odds of a woman reporting menstrual cycle irregularities 54% against a woman reporting a small level of stress. Infertility was also shown to be significant in this model, producing an odds ratio of 1.85. Finally, various variables indicating difficult menstrual cycles (heavy menstrual cycles and painful menstrual cycles) were shown to be significant in the model. Collinearity could exist between these two variables, as both variables included the word “prolonged” in the survey question, though two very different symptoms were being targeted by the variables -- heavy menstrual cycles aims to account for a high volume of blood lost during a menstrual cycle while painful menstrual cycles aims to examine the level of pain incurred during a menstrual cycle.

Table 9. Logistic regression analysis and adjusted odds ratios utilizing the expanded diabetes variable.

Variable	Beta Estimate	Odds Ratio	95% CI	Pr > ChiSq
Diabetes Diagnosis			--	--
Insulin resistant, glucose intolerant, or pre-diabetic	0.09	1.10	(0.67, 1.81)	0.71
Type I Diabetic	-0.28	0.75	(0.26, 2.22)	0.61
Type II Diabetic, Diet Only	**1.21**	**3.36**	**(1.19, 9.47)**	**0.02**
Type II Diabetic, Oral Pills Only	-0.04	0.96	(0.45, 2.09)	0.93
Type II Diabetic, Insulin Only	0.67	1.96	(0.58, 6.59)	0.28
Type II Diabetic, Oral Pills and Insulin	-0.26	0.77	(0.17, 3.55)	0.74
Unknown Diabetic	-0.14	0.87	(0.18, 4.10)	0.86
Non-Diabetic	*Ref*	--	--	--
Age, 1-year	**-0.02**	**0.98**	**(0.97, 0.99)**	**0.03**
BMI Category				
Underweight	0.16	1.17	(0.59, 2.33)	0.65
Normal Weight	*Ref*	--	--	--
Overweight	-0.14	0.87	(0.70, 1.07)	0.18
Insurance				
Medicare/Medicaid	0.05	1.05	(0.62, 1.76)	0.86
VA/Tricare	0.50	1.65	(0.85, 3.17)	0.14
Private Insurance	*Ref*	--	--	--
Uninsured	0.25	1.28	(0.95, 1.72)	0.10
Unknown	0.002	1.00	(0.38, 2.63)	1.00
Education Level				
High school diploma or less	0.02	1.02	(0.63, 1.65)	0.93
GED	0.02	1.02	(0.48, 2.20)	0.95
Vocational or training certificate	0.15	1.16	(0.71, 1.88)	0.56
Some college or associate’s degree	**0.24**	**1.27**	**(1.03, 1.56)**	**0.03**
Bachelor’s degree or higher	*Ref*	--	--	--
Other	0.07	1.07	(0.61, 1.87)	0.82

Table 9. Continued.

Level of Activity				
Sedentary	0.03	1.04	(0.76, 1.41)	0.82
Moderately Active	-0.03	0.97	(0.75, 1.25)	0.82
Very Active	*Ref*	--	--	--
General Health Condition				
Excellent	*Ref*	--	--	--
Very Good	0.02	1.02	(0.76, 1.35)	0.91
Good	0.20	1.22	(0.89, 1.68)	0.21
Fair	0.35	1.42	(0.95, 2.13)	0.09
Poor	0.46	1.59	(0.73, 3.45)	0.24
Current Stress Level				
Small	*Ref*	--	--	--
Moderate	0.12	1.13	(0.84, 1.52)	0.43
Large	0.27	1.30	(0.95, 1.79)	0.10
Overwhelming	**0.27**	**1.54**	**(1.03, 2.28)**	**0.03**
Problems Controlling Worry				
Yes, in the past 12 months	-0.12	0.88	(0.67, 1.17)	0.38
Yes, in my lifetime	-0.13	0.88	(0.69, 1.12)	0.31
No	*Ref*	--	--	--
Excessive Anxiety or Worry				
Yes, in the past 12 months	-0.16	0.85	(0.36, 2.02)	0.72
Yes, in my lifetime	-0.20	0.82	(0.35, 1.93)	0.65
No	*Ref*	--	--	--
Trying to Lose Weight	0.11	1.12	(0.91, 1.37)	0.28
Frequent Yeast Infections	-0.04	0.96	(0.71, 1.29)	0.78
General Pelvic Pain	0.22	1.24	(0.94, 1.64)	0.12
Infertility	**0.61**	**1.85**	**(1.30, 2.64)**	**0.0007**
Painful or Prolonged Menstrual Cycles	**0.27**	**1.31**	**(1.08, 1.60)**	**0.006**
PMS/PMDD	0.05	1.05	(0.81, 1.36)	0.74
Polycystic Ovarian Syndrome	**0.53**	**1.70**	**(1.21, 2.39)**	**0.002**
Prolonged/Heavy Menses	**0.36**	**1.44**	**(1.17, 1.76)**	**0.0006**
Severe Hot Flashes	**0.57**	**1.77**	**(1.27, 2.46)**	**0.0007**
Vaginal Dryness	**0.26**	**1.30**	**(1.04, 1.62)**	**0.02**
Vulvar Pain	0.31	1.36	(0.96, 1.95)	0.09
Other Gynecological Conditions	0.33	1.39	(0.83, 2.34)	0.21

Table 9. Continued.

Birth Control Level				
No birth control	*Ref*	--	--	--
Likely to provoke menstruation	-0.06	0.94	(0.76, 1.15)	0.54
Likely to eliminate menstruation	**0.74**	**2.10**	**(1.58, 2.80)**	**<.0001**
Not likely to impact menstruation	-0.11	0.90	(0.59, 1.36)	0.61

In this fully-adjusted logistic regression analysis using the expanded diabetes variable, age, infertility, prolonged or painful menstrual cycles, PCOS, prolonged or heavy menses, severe hot flashes, and vaginal dryness managed to achieve statistical significance. In the expanded diabetes variable, only type II diabetics controlled by diet alone managed to achieve significance..

Given the number of independent variables analyzed, these models could suffer from over-adjustment. Table 10 presents a reduced model utilizing key potential confounders (based on the literature) in the analysis, which include age, BMI, level of activity, current stress level, PCOS, and birth control level. Age has a significant effect on the prevalence of type II diabetes, which composes a majority of diabetes cases.[40-42] Age is also known to have a regulatory impact on menstrual cycles. BMI is well known to be associated with diabetes[41,43], and BMI was also been shown to be associated with irregular menstruation in adolescent girls in a 2014 Pakistani study.[44] Increased physical activity has been shown to have some connection to menstrual cycle regulation and frequency, though the physiological function creating such a phenomenon is not well understood.[45] Physical activity has also been shown to be highly associated with diabetes.[41,43] The influence of mental stress on menstruation is well-known, often leading to missed cycles. In diabetes, a 2017 study showed that mental stress is highly associated with unhealthy eating patterns in young adults, which, in turn, influence the prevalence of diabetes.[46] The relationship between diabetes and PCOS, as well as between menstrual cycle irregularities and PCOS, was discussed in the literature review. Birth control, in all its various forms, is pharmacological agent utilized not only to regulate conception, but also to control, provoke, or eliminate menstrual cycles. Birth control is also known to fluctuate blood glucose levels and "exacerbate DM."[47]

The dichotomous diabetes variable was utilized over the expanded diabetes variable because of low numbers of observations in cell counts in the expanded diabetes variable. In this model, almost all included variables had at least one stratum gain statistical significance. Of primary interest, the dichotomous diabetes variable was significant, indicating diabetic woman had 1.53 times the odds of self-reporting menstrual cycle irregularities versus non-diabetic women. Being sedentary was statistically significant, and increased odds of self-reporting menstrual cycle regularities compared to very active women, seemingly contradicting the lack of statistical significance for overweight women. This could suggest multicollinearity between the variables.

Table 10. Reduced logistic regression analysis, utilizing the dichotomous diabetes variable and key confounders.

Variable	Beta Estimate	Odds Ratio	95% CI	Pr > ChiSq
Diabetes Status	**0.42**	**1.53**	**(1.12, 2.07)**	**0.006**
Age	**-0.02**	**0.98**	**(0.97, 0.99)**	**0.003**
BMI Category				
Underweight	0.31	1.37	(0.81, 2.31)	0.24
Normal Weight	*Ref*	--	--	--
Overweight	0.04	1.04	(0.89, 1.21)	0.65
Level of Activity				
Sedentary	**0.27**	**1.31**	**(1.02, 1.67)**	**0.03**
Moderately Active	0.11	1.11	(0.90, 1.37)	0.32
Very Active	*Ref*	--	--	--
Current Stress Level				
Small	*Ref*	--	--	--
Moderate	0.21	1.24	(1.00, 1.54)	0.05
Large	**0.51**	**1.66**	**(1.32, 2.11)**	**<.0001**
Overwhelming	**0.74**	**2.10**	**(1.54, 2.88)**	**<.0001**
Polycystic Ovarian Syndrome	**0.77**	**2.16**	**(1.65, 2.83)**	**<.0001**

Table 10. Continued.

Birth Control Level				
No birth control	*Ref*	--	--	--
Likely to provoke menstruation	**-0.22**	**0.80**	**(0.70, 0.95)**	**0.01**
Likely to eliminate menstruation	**0.64**	**1.89**	**(1.50, 2.38)**	**<.0001**
Not likely to impact menstruation	-0.07	0.93	(0.64, 1.35)	0.71

In this reduced-adjusted logistic regression analysis, diabetes, age, stress level, PCOS, and birth control level were shown to be statistically significant..

Sensitivity Analyses

PCOS was shown to be very strongly significant in each of the logistic regression models. PCOS was not considered as an effect modifier within the context of this analysis due to unresolved questions regarding the direction of flow of the causal pathway between menstrual cycle regularities and the disease, as well as diabetes and the disease. The strength of the association, however, could indicate some influence in the causal pathway between diabetes and menstrual cycle irregularities. A reduced logistic regression analysis stratified by PCOS status can be found in the Appendix in Table 11 and Table 12. There is no literature to defend such a stratification, but the strength of the association from Table 8, Table 9, and Table 10, along with the physiology and hallmarks of the disease, created an interesting question that could contribute to discussions surrounding PCOS.

Table 11 presents the reduced adjusted logistic regression analysis for women reporting no PCOS diagnosis (n = 3,941). In this model, diabetes remained significant, decreasing slightly compared to the result from Table 10 to an odds ratio of 1.49 (compared to Table 10's 1.53). Stress is highly significant in the model, within even a slight increase in stress to moderate increasing the odds of a woman self-reporting menstrual cycle irregularities by 31% when compared to a woman with a small level of stress.

The reduced adjusted logistic regression analysis for women reporting a PCOS diagnosis (n=304) can be found in Table 12. In this model, all variables in the reduced analysis lose statistical significance, with the exception of age. Odds of self-reporting menstrual cycle irregularities among diabetic women increase to 1.76 times that of non-diabetic women, compared to the 1.49 odds found in Table 11 in the same comparison group. The effect of age on self-reporting menstrual cycle irregularities is slightly more protective than in Table 12. Curiously, stress, which was highly significant in the population reporting no menstrual cycle irregularities, is highly insignificant in this population, with overwhelming stress showing a protective effect. This could primarily be due to a small number of observations in this particular cell (n = 35, composing 11.51% of the population of women reporting a PCOS diagnosis). Also of interest is that birth control, regardless of categorization, is shown to be protective across all strata.

The results of this analysis indicate a fascinating relationship between the variables and PCOS status, indicating an interesting direction for future research. Adding the gynecological conditions found in the fully adjusted models in Table 8 and Table 9 could yield a significantly different result. It is also important to consider that many of the results in Table 12 could be due to small numbers in cell counts in the data, especially when considering that the sample population measured for this analysis consisted of only 304 subjects.

DISCUSSION

Overall, the results of this analysis yielded conflicting and inconclusive results in this evaluation of the relationship between diabetes and menstrual cycle regularity status. The logistic regression analyses in Table 8 and Table 9, accounting for all identified potential confounders, did not show a significant association between diabetes and menstrual dysregulation. Many of the gynecological conditions are highly correlated, and reporting one condition could lead to reporting others; for instance, a woman reporting general pelvic pain could also be reporting other gynecological conditions, which could result in biased estimates from the model. The reduced logistic regression analysis in Table 10, however, showed diabetes being statistically significant. The bivariate odds ratios in Table 1 and Table 5 also showed a strong relationship between diabetic status and menstrual cycle irregularities. The findings in Table 1, Table 5, and Table 10 are all consistent with findings in the 1992 Danish study[15], a 2003 study[17], and a 2010 Greek study.[18]

The expanded diabetes variable in the fully-adjusted logistic regression analysis in Table 9, however, showed one subtype of diabetes (Type II diabetes controlled through diet only) as significantly associated with menstrual dysregulation. This result is possibly consistent with the findings from the 1995 Yeshaya and colleagues study[16] and a 2010 Chilean study[20] that found that menstrual disturbances were found only among women with poorly controlled diabetes. These women are only treating their diabetes through lifestyle choices, which may suggest poorer control of the disease in these women than among women who do utilize pharmacological treatment. On the other hand, it may indicate less severe diabetes. However, it is important to remember that there are a very small number of observations analyzed in this particular cell; the statistical power may not be adequate to make such a determination.

Age was found to be protective against irregular menstrual cycles in Table 8, Table 9, and Table 10, which is consistent with common knowledge regarding the regulatory impact of age on menstrual cycles. Birth control likely to eliminate menstrual cycles was also significant in all three models, with an odds ratio of 2.10 in Table 8 and Table 9 for a woman taking a birth control method likely to eliminate menstrual cycles compared to a woman not taking birth control. In Table 10, these odds decreased to 89% greater among women taking a birth control method likely to eliminate menstrual cycle compared to women not taking birth control. Table 10 also indicated a significant decrease in odds of self-reporting irregular menstrual cycles among women taking a birth control method likely to provoke menstrual cycles compared to women taking no birth control.

Being overweight was shown to be protective in all three models, though failed to achieve statistical significance in any of the models. There are many possible explanations for this particular result. It is important to remember that, inherently, BMI does not account for muscle mass, and so women with a high volume of muscle mass could be incorrectly categorized. Birth control could also be another explanation. A chi-square analysis of the categorical BMI variable and the birth control level variable showed high correlation (p-value <.0001). 55.72% of overweight women reported using no birth control, compared to 49.72% of women with a normal BMI and 54.41% of women categorized as underweight. A larger percentage of overweight women were utilizing a birth control method not likely to impact menstruation than normal weight or underweight women (5.30% for overweight women, compared to 2.33% for normal weight women and 1.47% for underweight women). Overweight women were also more likely to use a method of birth control likely to eliminate menstrual cycles than underweight or normal weight women (prevalence ratios of 1.42 and 1.12, respectively). Another explanation could be strong associations with comorbid gynecological conditions of BMI. For example, 12.59% of overweight women also reported a PMS or PMDD diagnosis compared to 8.33% of underweight women and 7.57% of normal weight women (p-value <.0001). Similarly, 10.40% of overweight women also reported a PCOS diagnosis while

3.08% of normal weight women and 2.78% of underweight women reported the condition (p-value <.0001).

Finally, the significance of variables such as age, severe hot flashes, and vaginal dryness in the fully-adjusted models in Table 8 and Table 9 could indicate poor control for menopause in the models. The average age for perimenopause (45)[29] was utilized as the control for menopause after indication that menopause outcomes in the dataset were rather unstable. Though the control for menopause may have been appropriate, these symptoms may indicate that the method for control was not adequate. A different control methodology for menopause could yield significantly different results. A fully-adjusted logistic regression analysis with women reporting severe hot flashes, most commonly associated with menopause, eliminated from the sample population can be found in the Appendix in Table 13. There are other conditions that can cause severe hot flashes, such as thyroid disorders, but this provided another proxy for control of menopause in the sample.

After further restricting the population to eliminate women reporting severe hot flashes as another proxy for menopause status, the sample contained 4,002 observations. Within this population, 1,060 women reported menstrual cycle irregularities (p-value <.0001) and 220 women reported diabetes (p-value <.0001). The average age of this sample, overall, was 33.50 (SD 6.71) and the average BMI was 27.81 (SD 7.56). Curiously, the population in this analysis is even more well-educated than the study population, as designed in the methods, with the largest percentage of women in this population reporting post-graduate training (36.43%), and the second largest percentage indicating possession of a bachelor's degree (29.47%).

In this model, the removal of women indicating severe hot flashes created a rather dramatic alteration in the odds found in Table 8 and Table 9, with the odds a diabetic woman in this study population having 1.51 times the odds of self-reporting menstrual cycle irregularities compared to a non-diabetic woman. This analysis, when compared to the results of Table 8 and Table 9, indicates that control for menopause in the study population may not have been adequate to account for the population of pre-menopausal or menopausal women in this population. Further analysis and examination is needed to control and modify such a population.

The primary strength of this analysis were the unique variables within the dataset. A variable categorizing diabetic status into many levels provided unique insight into diabetes within this analysis. The variable allowed examination of several different types and treatments of diabetes, though low cell counts in many of the strata limited analyses. This variable created a unique opportunity to evaluate a population beyond dichotomous variables and gain insight into associations and possible mechanistic relationships. The population studied in this analysis was also large, providing increased statistical power to these analyses and providing insight into an understudied population regarding this question. This study also included an in-depth characterization of women's health issues among this population of women. A careful analysis of potential confounders for this question within this population also provided more strength to this population.

The dataset does suffer from a significant amount of selection bias based on the population chosen for analysis from KWHR and selection bias. Furthermore, the population within this analysis is more white and more educated than the general population, and, thus, is not generalizable to a more general population. Limited information on variables and observations could be leading to misinterpretation of results and observations. Irregular menstruation, for instance, is defined by several different dysfunctions in menstrual cycles.[4] The codebook does not define how such a variable was defined to the survey takers, or if the survey takers assigned their own definition to the variable when self-reporting such status. The length of cycle variable also presents an interesting conundrum when considering menstrual cycle regularity status, as the lowest grouping of time for the variable is 2 months or less, which could result in women with irregular menstrual cycles being categorized in the referent group. The observations and classification was also dependent upon accurate self-reporting. Women who are not aware they possess certain conditions may be causing unknown misclassification bias in this population. Other measures, such as BMI, rely entirely on self-reported data, and so the data may not reflect the reality for many women in this population. Furthermore, cross-sectional studies cannot determine causation, and thus can only speak of associations rather than provide insight into mechanistic relationships regarding menstrual cycle status and diabetes.

CONCLUSION

A strong association was consistently shown between diabetes and menstrual cycle irregularities in all the analyses, despite several analyses lacking statistical significance. Identifying multicollinearity, adjusting the model, and better identifying and analyzing potential indicators of menopause status could yield significantly different results in the analysis. In the expanded diabetes variable, type II diabetics controlling through diet alone were shown to be significant, even in the fully-adjusted model, indicating an interesting relationship that could be explored in further study. Small numbers within this category, however, could have a significant effect on the strength, requiring this result to considered with caution.

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APPENDIX

Logistic Regression Analyses Stratified by PCOS Status

Table 11. Reduced adjusted logistic regression analysis and adjusted odds ratios, utilizing the dichotomous diabetes variable and stratified for women reporting no PCOS diagnosis.

Variable	Beta Estimate	Odds Ratio	95% CI	Pr > ChiSq
Diabetes Status	**0.40**	**1.49**	**(1.04, 2.14)**	**0.03**
Age	**-0.01**	**0.99**	**(0.97, 1.00)**	**0.01**
BMI Category				
Underweight	0.41	1.51	(0.89, 2.56)	0.13
Normal Weight	*Ref*	--	--	--
Overweight	0.04	1.04	(0.88, 1.22)	0.65
Level of Activity				
Sedentary	**0.28**	**1.32**	**(1.02, 1.70)**	**0.04**
Moderately Active	0.10	1.11	(0.89, 1.37)	0.35
Very Active	*Ref*	--	--	--
Current Stress Level				
Small	*Ref*	--	--	--
Moderate	**0.27**	**1.31**	**(1.04, 1.65)**	**0.02**
Large	**0.55**	**1.73**	**(1.35, 2.21)**	**<.0001**
Overwhelming	**0.86**	**2.36**	**(1.70, 3.29)**	**<.0001**
Birth Control Level				
No birth control	*Ref*	--	--	--
Likely to provoke menstruation	**-0.22**	**0.80**	**(0.67, 0.96)**	**0.02**
Likely to eliminate menstruation	**0.70**	**2.02**	**(1.59, 2.56)**	**<.0001**
Not likely to impact menstruation	0.07	1.07	(0.73, 1.57)	0.73

In this reduced logistic regression analysis stratified by no PCOS status, diabetes, age, activity level, stress level, and birth control level were all shown to be statistically significant.

Table 12. Reduced adjusted logistic regression analysis and adjusted odds ratios, utilizing the dichotomous diabetes variable and stratified for women reporting a PCOS diagnosis.

Variable	Beta Estimate	Odds Ratio	Chi-Square	Pr > ChiSq
Diabetes Status	0.57	1.76	(0.97, 3.18)	0.06
Age	**-0.05**	**0.95**	**(0.91, 1.00)**	**0.03**
BMI Category				
Underweight	-14.13	<.001	(<.001, >999.999)	0.99
Normal Weight	*Ref*	--	--	--
Overweight	-0.21	0.81	(0.42, 1.58)	0.54
Level of Activity				
Sedentary	0.39	1.48	(0.56, 3.88)	0.43
Moderately Active	0.31	1.36	(0.56, 3.28)	0.50
Very Active	*Ref*	--	--	--
Current Stress Level				
Small	*Ref*	--	--	--
Moderate	-0.28	0.76	(0.34, 1.68)	0.50
Large	0.23	1.25	(0.54, 2.91)	0.60
Overwhelming	-0.07	0.93	(0.32, 2.77)	0.90
Birth Control Level				
No birth control	*Ref*	--	--	--
Likely to provoke menstruation	-0.16	0.85	(0.48, 1.52)	0.59
Likely to eliminate menstruation	-0.29	0.75	(0.29, 1.95)	0.55
Not likely to impact menstruation	-1.24	0.29	(0.07, 1.14)	0.08

In this analysis, age was the only variable that managed to achieve statistical significance. The association with diabetes in this analysis was larger than the association in Table 11.

Logistic Regression Analysis Eliminating Severe Hot Flashes

Table 13. Reduced-adjusted logistic regression analysis for sample population excluding women reporting severe hot flashes, utilizing the dichotomous diabetes variable.

Variable	Beta Estimate	Odds Ratio	95% CI	Pr > ChiSq
Diabetes Status	**0.41**	**1.51**	**(1.09, 2.08)**	**0.01**
Age	**-0.02**	**0.98**	**(0.97, 0.99)**	**0.002**
BMI Category				
Underweight	0.27	1.31	(0.76, 2.26)	0.33
Normal Weight	*Ref*	--	--	--
Overweight	0.05	1.05	(0.89, 1.24)	0.54
Level of Activity				
Sedentary	**0.26**	**1.30**	**(1.00, 1.68)**	**0.05**
Moderately Active	0.13	1.14	(0.92, 1.42)	0.23
Very Active	*Ref*	--	--	--
Current Stress Level				
Small	*Ref*	--	--	--
Moderate	0.22	1.24	(0.99, 1.56)	0.06
Large	**0.47**	**1.60**	**(1.25, 2.04)**	**0.0002**
Overwhelming	**0.69**	**2.00**	**(1.43, 2.78)**	**<.0001**
Polycystic Ovarian Syndrome	**0.78**	**2.19**	**(1.66, 2.89)**	**<.0001**
Birth Control Level				
No birth control	*Ref*	--	--	--
Likely to provoke menstruation	**-0.22**	**0.80**	**(0.67, 0.95)**	**0.01**
Likely to eliminate menstruation	**0.67**	**1.95**	**(1.54, 2.47)**	**<.0001**
Not likely to impact menstruation	-0.15	0.86	(0.57, 1.29)	0.46

In this analysis, diabetes, age, stress level, PCOS, and birth control level were shown to be significant. Diabetes showed a strong association with menstrual cycle regularities in this adjusted analysis.

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